

**DERWENT-ACC-NO:** 2001-541522**DERWENT-WEEK:** 200654*COPYRIGHT 2009 DERWENT INFORMATION LTD*

**TITLE:** Nasal formulation to treat e.g.  
osteoporosis comprises calcitonin as  
active ingredient and specified  
concentration of citric acid or its  
salt

**INVENTOR:** STERN W**PATENT-ASSIGNEE:** UNIGENE LAB INC[UNIGN]

**PRIORITY-DATA:** 2000US-180241P (February 4, 2000) ,  
2001US-776537 (February 2, 2001)

**PATENT-FAMILY:**

<b>PUB-NO</b>	<b>PUB-DATE</b>	<b>LANGUAGE</b>
WO 0156594 A1	August 9, 2001	EN
AU 200136604 A	August 14, 2001	EN
US 6440392 B1	August 27, 2002	EN
EP 1251867 A1	October 30, 2002	EN
CN 1422160 A	June 4, 2003	ZH
CN 1183965 C	January 12, 2005	ZH
AU 783952 B2	January 5, 2006	EN

**DESIGNATED-STATES:** AE AG AL AM AT AU AZ BA BB BG BR BY  
 BZ CA CH CN CR CU CZ DE DK DM DZ EE  
 ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT  
 LU LV MA MD MG MK MN MW MX MZ NO NZ  
 PL PT RO RU SD SE SG SI SK SL T J  
 TM TR TT TZ UA UG UZ VN YU ZA ZW AT  
 BE CH CY DE DK EA ES FI FR GB GH GM  
 GR IE IT KE LS LU MC MW MZ NL OA PT  
 SD SE SL SZ TR TZ UG ZW AL AT BE CH  
 CY DE DK ES FI FR GB GR IE IT LI LT  
 LU LV MC MK NL PT RO SE SI TR

**APPLICATION-DATA:**

<b>PUB-NO</b>	<b>APPL- DESCRIPTOR</b>	<b>APPL-NO</b>	<b>APPL-DATE</b>
WO2001056594A1	N/A	2001WO- US03212	January 31, 2001
AU 200136604A	N/A	2001AU- 036604	January 31, 2001
AU 783952B2	N/A	2001AU- 036604	January 31, 2001
CN 1422160A	N/A	2001CN- 807605	January 31, 2001
CN 1183965C	N/A	2001CN- 807605	January 31, 2001
EP 1251867A1	N/A	2001EP- 908769	January 31, 2001
EP 1251867A1	N/A	2001WO- US03212	January 31, 2001
US 6440392B1	Based on	2001US- 776537	February 2, 2001

**INT-CL-CURRENT:**

TYPE	IPC DATE
CIPP	A61K38/23 20060101
CIPS	A61K38/23 20060101
CIPS	A61K9/00 20060101

**ABSTRACTED-PUB-NO:** WO 0156594 A1

**BASIC-ABSTRACT:**

NOVELTY - Liquid pharmaceutical composition (I) suitable for nasal administration comprises calcitonin or its acid addition salt and citric acid or its salt in a concentration of 10 - 50 mM.

DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of improving the bioavailability or the concentration of plasma calcitonin in a subject following nasal administration.

None given.

USE - To treat osteoporosis, Paget's disease and malignant hypercalcemia.

Wistar rats were administered intranasally 20  $\mu$ l of salmon calcitonin (rsCT) (200  $\mu$ g/ml) in 0.85% sodium chloride, Tween 80 (0.1%), phenylethyl alcohol (0.2%), benzyl alcohol (0.5%) and varying amounts of citric acid adjusted to pH 3.7 at time = 0, 20, 60 and 90 minutes. No results were given. At 0 mM citric acid, the bioavailability (B) was  $0.89 \pm 0.19$  and maximum SCT plasma (P) was  $1.1 \pm 0.52$ . At 100 mM citric acid, (B) was  $13.36 \pm 3.38$  and (P) was  $12.98 \pm 3.96$ . The results show that the bioavailability and peak concentration of rsCT was a function of the concentration of citric acid in the formulation.

ADVANTAGE - The composition, unlike the prior art, has

improved stability and bioavailability of plasma calcitonin required for nasal application.

## **EQUIVALENT-ABSTRACTS:**

### **PHARMACEUTICALS**

Preferred Composition: (I) further comprises an aqueous liquid nasal carrier; at least 0.1 wt.% Tween 80 and at least one preservative selected from benzyl alcohol, phenylethyl alcohol, methyl parabens, ethyl parabens, propyl parabens or butyl parabens. The carrier comprises aqueous saline. The composition is a nasal spray and has a viscosity of less than 0.98 cP. (I) has a pH of about 3 - 5 (preferably 3.5 - 3.9 especially 3.7) and an osmotic pressure of about 250 - 350 mOsm/l.

Preferred Calcitonin: The calcitonin is selected from salmon calcitonin, human calcitonin, porcine calcitonin or 1,7-Asu-eel calcitonin (preferably salmon calcitonin). The calcitonin or its salt is present in about 100 - 8000 (preferably 500 - 4000, especially 500 - 3000, particularly 1000 - 2500) MRC units/ml of the composition.

Preferred Formulation: (I) comprises salmon calcitonin (about 2200 MRC units), about 10 (preferably 20) mM citric acid, phenylethyl alcohol (about 0.2%), benzyl alcohol (about 0.5%) and Tween 80 (about 0.1%).

The composition is administered nasally.

None given.

**TITLE-TERMS:** NASAL FORMULATION TREAT OSTEOPOROSIS  
COMPRISE CALCITONIN ACTIVE INGREDIENT  
SPECIFIED CONCENTRATE CITRIC ACID SALT

**DERWENT-CLASS:** B04

**CPI-CODES:** B04-J04A; B10-C02; B12-M01B; B14-N01;

**CHEMICAL-CODES:** Chemical Indexing M1 \*01\*  
 Fragmentation Code D011 D601 F012 F014  
 F423 F521 G010 G013 G100 H1 H100 H101  
 H181 H182 H4 H401 H441 H481 H5 H598 H8  
 H9 J0 J011 J012 J1 J111 J171 J172 J3  
 J311 J371 K0 K2 K224 L2 L250 M210 M211  
 M271 M280 M281 M311 M312 M313 M314  
 M315 M320 M321 M322 M331 M332 M333  
 M340 M342 M343 M349 M371 M381 M391  
 M392 M423 M431 M510 M511 M520 M521  
 M530 M531 M540 M620 M782 P714 R012  
 Specific Compounds R01874 Registry  
 Numbers 89804

Chemical Indexing M1 \*03\*  
 Fragmentation Code F011 F012 F014 F019  
 F423 F499 F521 G013 G100 H1 H101 H183  
 H2 H212 H4 H405 H441 H484 H498 H8 H9  
 J0 J014 J1 J171 J3 J312 J373 K0 L2  
 L250 M280 M311 M312 M313 M314 M315  
 M322 M323 M331 M332 M333 M340 M342  
 M343 M349 M371 M381 M392 M393 M423  
 M431 M510 M523 M531 M540 M782 P714  
 R012 Specific Compounds RA1ZBA  
 Registry Numbers 89818

Chemical Indexing M1 \*04\*  
 Fragmentation Code F011 F012 F014 F019  
 F423 F499 F521 G010 G013 G019 G100 H1  
 H101 H182 H2 H212 H4 H405 H441 H484  
 H498 H5 H598 H8 H9 J0 J014 J1 J171 J3  
 J312 J373 M210 M211 M271 M281 M311  
 M312 M313 M314 M315 M321 M323 M331  
 M332 M333 M340 M342 M343 M349 M371  
 M381 M393 M423 M431 M510 M523 M533  
 M540 M782 P714 R012 Specific Compounds  
 RA24LZ Registry Numbers 89815

Chemical Indexing M1 \*07\*

Fragmentation Code F012 F013 F014 F113  
H4 H403 H483 H5 H522 H589 H7 H721 H8  
J0 J011 J2 J271 K0 L8 L814 L821 L833  
M225 M231 M262 M281 M312 M323 M332  
M342 M343 M373 M383 M391 M393 M423  
M431 M510 M521 M530 M540 M782 R012  
Specific Compounds R01870 Registry  
Numbers 104479 135417

Chemical Indexing M2 \*02\*  
Fragmentation Code H4 H401 H481 H8 J0  
J013 J1 J173 M280 M313 M321 M332 M344  
M349 M381 M391 M416 M431 M620 M782  
Q620 R012 Specific Compounds R00419  
R07029 Registry Numbers 104520 129792  
129991 130395 132222 133510 140723  
140725 159060 191428 2471 250717  
278358 278359 3589 849 87079 95073  
95095 99996

Chemical Indexing M2 \*05\*  
Fragmentation Code G010 G100 H4 H401  
H481 H8 M280 M312 M321 M332 M342 M373  
M391 M414 M431 M510 M520 M531 M540  
M782 Q620 R012 Specific Compounds  
R00199 Registry Numbers 10035

Chemical Indexing M2 \*06\*  
Fragmentation Code G010 G100 H4 H401  
H481 H8 M280 M311 M321 M342 M373 M391  
M414 M431 M510 M520 M531 M540 M782  
Q620 R012 Specific Compounds R00714  
Registry Numbers 50

Chemical Indexing M6 \*08\*  
Fragmentation Code P714 Q620 R012 R111  
R252 R315

**UNLINKED-DERWENT-REGISTRY-  
NUMBERS:**

; 0199U ; 0419U ;  
0714U ; 1870U ; 1874U

**SECONDARY-ACC-NO:**

**CPI Secondary Accession Numbers:** 2001-161633